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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/656,084	09/06/2000	Barry N. Kreiswirth	19124.0002	8869

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EXAMINER
LY, CHEYNE D

ART UNIT	PAPER NUMBER
1631	21

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/656,084	KREISWIRTH ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 21, 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 3-5, 7, 8, 10-14, 21-36, and 38-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 7, 8, 10-14, 21-36, and 38-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' arguments in Paper No. 20, filed May 21, 2003, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. Applicants' Declaration Under 37 C.F.R. § 1.132 has been accepted.

3. The cancellation of claims 6, 9, and 37 has been acknowledged.

4. The addition of new claims 38-41 has been acknowledged.

CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH

5. Claims 15-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

6. This rejection is maintained with respect to claims 15-18, as recited in the previous office actions Paper No. 10, mailed April 05, 2002; and 17, mailed January 27, 2003.

7. Applicants' pointed to support in the specification which Applicants claim to provide adequate disclosure for enabling one of ordinary skill to practice the invention as directed to generating the following "costs" as recited in claims 15-18: relative cost, absolute cost, repeat motif cost, point mutation cost, and total cost (which is based upon the summation of the repeat cost and point mutation cost) has been fully considered. The pointed support in

the specification has been found to be not persuasive, therefore, does not provide sufficient guidance to enable one of ordinary skill in the art to practice the invention.

8. Specific to "absolute costs", "relative costs", "repeat mutation costs" and "point mutation costs", the pointed to support, page 30, line 14, through page 33, line 1; page 30, line 7, through page 33, line 1; page 8, line 22, through page 9, line 6, has been fully considered and found to be not persuasive because the descriptions do not provide sufficient guidance for one of ordinary skill in the art to practice the claimed invention.

9. Applicants discloses the software of the present invention treats insertion or deletion of a cassette as a single event, therefore, might recognize sequence #1 as being related to #3 due to the insertion of 3 cassettes (page 31, lines 14-19). Further, comparing two sequences directly, an absolute cost can be calculated for each sequence (page 32, lines 5-7). The repeat motifs are analyzed in terms of the number of insertions and deletions of whole cassettes and the relative cost is calculated based on the similarity of the repeat motifs (page 31, lines 20-24). The point-mutation cost is calculated based on the similarity of individual base pairs, not on the basis of the repeat motif (page 32, lines 8-11). The instant specification only defines "absolute costs", "relative costs", "repeat mutation costs" or "point mutation costs" as they are directed to sequence similarities, but never actually provide guidance to one of ordinary skill in the art to perform the steps to generate the various costs from the sequence comparisons. It is acknowledged that the instant specification provides an equation for calculating Relatedness R (page 33, line 1) and the parameters for the said equation are also defined (page 32, line 15-25). However, Applicants do not disclose how the Relatedness R equation is used to calculate the defined "absolute costs", "relative costs", "repeat mutation

costs" or "point mutation costs". Further, the instant specification suggests that the calculation of the various costs requires assigning values for each of the required parameters in an equation for determining the said costs. The instant specification only defines the various costs without providing guidance as to how such the values associated with the costs are actually determined. Such definitions fall short of providing sufficient guidance that would enable one of ordinary skill in the art to practice the instant invention.

10. Further, Applicants argue that the methods of cost analysis are familiar to one of ordinary skill in the art. The said argument has been fully considered and found to be unpersuasive. Applicants.disclose "conventional software does not adequately determine relatedness between sequences" and the instant claimed invention overcomes such inadequacies by calculating the "absolute costs" and "relative costs" when comparing sequences (page 30, lines 21-24 to page 31, line 1). Therefore, it is suggested by Applicants that the determination of "absolute costs" and "relative costs" as directed to the instant invention is not well known in the art.

NEW CLAIM REJECTIONS - 35 USC § 112 SECOND PARAGRAPH

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1, 3-5, 7, 8, 10-14, 21-36, and 38-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. This rejection is necessitated by Applicants' amendments.

14. Claim 1, lines 12; claim 39, line 10, claim 40, line 10, recite a step for identifying infected patients or objects. While, claim 1, lines 14-15; claim 39, line 12; and claim 40, line 12, recite a step for tracking infected patients and objects. The conflicting limitations of requiring both infected patients or objects; and infected patients and objects cause the claims to be vague and indefinite. Clarification of the metes and bounds is required. Claims 3-5, 7, 8, 10-14, 21-36, 38 and 41 are rejected for being directly or indirectly dependent from claim 1, 39, or 40.

NEW CLAIM REJECTIONS - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 3-5, 12-14, 21, 25-30, 32-34, 36, 39-41 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Hoe et al. (April 1999).

17. This rejection is necessitated by Applicants' amendments.

18. Hoe et al. discloses a method for tracking pathogenic microbial species in an epidemiologic investigation of putative disease outbreaks (page 254, column 1, lines 1-14) and providing insight to the virulence of the said microbial species (page 261, column 1, lines 51-53 to column 2, lines 1-15), as in instant claims 25-27. The method of Hoe et al. comprises sequencing the *sic* gene wherein a region contains repeat sequences to unambiguously differentiate 30 M1 isolates recovered from 28 patients in Texas (Abstract etc.). The sequenced nucleic acid molecules are used to search an *emm* database maintained

in the laboratory (page 255, column 2, Sequence Analysis of *emm* §, lines 3-10 and Figure 4), as in instant claims 28-30. M1 isolates cultured from patients share a common ancestor and lack readily detectable chromosomal variation (page 254, column 2, lines 2-13 and Figure 1), as in instant claims 1, 5, 36, and 39-41.

19. It is noted that the laboratory of Hoe et al. is located in Texas, therefore, suggests that the database and the location where the sample is obtained from patients in Texas are in the same location, as in instant claim 4.

20. Further, the database contains sequences from global sources (page 255, lines 28-30) and GenBank, Bethesda, MD, (Figure 1) which is remote from the location where the location of the samples are obtained, as in instant claims 3 and 21.

21. The inclusion of a document by Benson et al. is not used as prior art but only to disclose that sequences from GenBank are transmitted via a network from a remote facility with a centralized database (page 4, column 1, Building The Database § and Figure 3) and transmission exchanges occur between research remote infection control facility such as Baylor College of Medicine (Hoe et al., Figure 1) and NCBI (Benson et al., BLAST sequence similarity searching §), as in instant claims 12 and 32.

22. Further, Benson et al. discloses the GenBank and *Entrez* are available over the Internet in a client server version or GenBank in a CD-ROM (Benson et al., page 5, column 1, lines 14-32), as in instant claim 33.

23. The sample is amplified by PCR and sequenced (page 258, column 1, lines 1-7; and page 259, PCR and Sequence Analysis of a Polymorphic Direct Repeat (DR) Chromosomal Region §), as in instant claims 13 and 14.

24. Many *sic* alleles are confined to local geographic areas, however, several alleles were found among organisms cultured from patients in Mexico and former East Germany (page 261, column 2, lines 16-23), as in instant claim 34.

NEW CLAIM REJECTIONS - 35 USC § 103

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 1, 3-5, 7, 8, 10-14, 21-36, and 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoe et al. (1999) in combination with Frenay et al. (1996) taken with O'Brien et al (1997) in view of Paradiso et al. (PN US 6,404 340 B1).

28. This rejection is necessitated by Applicants' amendments.

29. Hoe et al. discloses the limitations of claims 1, 3-5, 12-14, 21, 25-30, 32-34, 36, 39-41 as described above.

30. Hoe et al. further discloses, "lack of readily available detectable chromosomal variation has limited insights on the molecular origin of new virulent strains" (page 254, column 2, lines 7-13), which suggests slowly mutating nucleic acid region. "Stockbauer et al. Analyzed 165 M1 isolates from diverse localities...and documented a uniquely high level of allelic variation" (page 255, column 1, lines 1-4), which suggests more rapidly mutating nucleic acid region. Therefore, the disclosure above suggests tracking of infection based on slowly and rapidly mutating nucleic acid region as in instant claim 31.

31. However, Hoe et al. does not disclose the bacterium as being Staphylococcus aureus and the first region is located in the protein A, as claims 7 and 8; patient medical history exchange as recited in instant claims 10, 11, 35, and 38, and patient tracking as recited in instant claims 22-24.

32. Frenay et al. discloses a method for an epidemiology study of infectious diseases wherein the source of the said infection is the Staphylococcus aureus on the basis of Protein A gene polymorphism. DNA sequencing of Staphylococcus aureus repeat sequences is performed (Abstract etc.), as in claim 7.

33. O'Brien et al. teaches a method of comparing "genetic relatedness among Mycobacterium tuberculosis isolates recovered from patients with active disease" (Page 387, Column 2, Lines 2-5). Due to the tracking of patients' medical records by Bellevue Hospital and the Department of Health in New York City, patients found not adhering to therapy were quarantined (page 389 to 390, Case Report §). This displays tracking a patient's physical location as well as the sharing of patient information as recited in instant claims 11 and 22.

Further, O'Brien et al. discloses a linked database of fingerprints from isolates in patients from New York City (page 391, column 1, 38-40), as in instant claim 23.

34. Patient is identified and patient sample analyzed prior confinement in the health care facility (page 389 to 390, Case Report §) as recited in instant claims 8 and 38.

35. The "clinical and demographic features of these patients" (Page 390, column 2, 1st paragraph) were reviewed for population risk factors in addition to determining "ongoing transmission of tuberculosis" (Page 390, column 2, lines 1-19) as recited in claim 10.

36. Paradiso et al. discloses a method for sensing and tracking a patient's physical location during a medical treatment for a specific disease (column 2, lines 32-49), as instant claim and 24.

37. It is noted that Hoe et al. discloses a general genetic approach to tracking disease outbreaks in epidemiologic investigations (page 254, column 1, lines 1-4) by analyzing samples from patients (Abstract etc.), thus, suggests that the method of Hoe et al. can be directed to tracking any disease outbreak specific to a patient population.

38. Hoe et al. discloses a method for tracking a disease outbreak (epidemiologic) by molecular characterization of a pathogenic microbial species through sequencing (page 254, column 1, lines 1-4). While, Frenay et al. discloses a method for tracking a Staphylcoccus aureus disease outbreak (epidemics) by molecular characterization of distinct sequence repeats (page 60, column 1, lines 1-7 to column 2, lines 1-15). One of ordinary skill in the art at the time of the instant invention would have been motivated to track the disease outbreak resulted from Staphylcoccus aureus as taught by Hoe et al. and Frenay et al.

39. O'Brien discloses a method for tracking a disease outbreaks (epidemics) of *Mycobacterium tuberculosis* by linking patients to the said outbreaks (Abstract etc.) via tracking a patients' physical location (page 389 to 390, Case Report §). While, Paradiso et al. discloses the method of tracking patients via sensing the patients' physical location during a medical treatment for a specific disease (column 2, lines 32-49). One of ordinary skill in the art at the time of the instant invention would have been further motivated to track outbreaks of Staphylcoccus aureus as taught by Hoe et al. and Frenay et al. by tracking infected patients in the outbreak as taught by O'Brien and Paradiso et al.

40. Therefore, it would have been obvious to one of ordinary skill in the art to perform the method of tracking outbreaks as taught by Hoe et al. and Frenay et al. by tracking infected patients in the outbreak as taught by O'Brien and Paradiso et al.

CONCLUSION

41. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

42. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

43. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

44. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

45. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

46. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
8/7/03

Ardin H. Marschel
ARDIN H. MARSCHEL
PRIMARY EXAMINER